Co-formulants/Non-active Substances Contained in Plant Protection Products or Biocidal Products in the European Union: Information Required on Co-formulants/Non-active Substances and Impact on the Authorisation of Products

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Since an application for the approval of an Active Substance (AS) shall include a dossier on the AS together with a dossier on at least one product, under both the Plant Protection Product (PPP) Directive 91/414/EEC and the Biocidal Product (BP) Directive 98/8/EC, information on co-formulants/non-active substances contained in products was required. Such information is also required under the PPP Regulation 1107/2009 and the BP Regulation 528/2012. In this article, required information on co-formulants/non-active substances contained in PPPs or BPs, impact on the authorisation of products that may be brought about by concerns related to the co-formulants/non-active substances, *etc*. are summarised.

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Introduction

In the European Union (EU), the submission of a dossier (documents and data package of the application) on at least one product was required for an application for the approval of an active substance (AS) under both the Plant Protection Product (PPP) Directive concerning the placing of PPPs on the market, which was for the products used for agricultural purposes, and the Biocidal Product (BP) Directive concerning the placing of BPs on the market, which was for the products used for non-agricultural purposes. Therefore, information on co-formulants/non-active substances contained in the product was submitted at the time of submission of application for the approval of ASs both under the PPP Directive and the BP Directive. The information is also required under the PPP Regulation and the BP Regulation, which were published to replace the PPP Directive and the BP Directive, respectively.

Under the PPP Regulation, a list of co-formulants which are not accepted for inclusion in PPPs is provided in Annex III. The list of co-formulants which are not accepted for inclusion in PPPs was established by the Amendment Regulation published in 2021, and then authorisation of products requires that products do not contain co-formulants included in this list.

Under the BP Regulation, provision of Union Authorisation was introduced.

Due to these new provisions introduced in the PPP Regulation and the BP Regulation, concerns related to the co-formulants/non-active substances contained in PPPs or BPs have come to have an impact on the authorisation of products.

Sumika Technoservice Corporation has been investigating regulatory information on approval/renewal of approval of ASs of PPPs or BPs in the EU for many years, and has recently investigated information on the Union Authorisation of BPs as well. We have started to provide support for investigations on information on co-formulants/non-active substances that may affect product authorisations needed to be granted after approval/renewal of approval of ASs. Based on our accumulated experience, this article summarises the information required for co-formulants/non-active substances contained in PPPs or BPs, as well as recent movements related to the impact of concerns related to co-formulants/non-active substances on the authorisation of products.

Provisions related to co-formulants/non-active substances in relation to the evaluation for approval/renewal of approval of ASs in PPPs/BPs or authorisation/renewal of authorisation of products in the EU

1. Provisions related to authorisations of products and provisions related to co-formulants/non-active substances under the PPP/BP Directives and the PPP/BP Regulations

The Directive 91/414/EEC[1] concerning the placing of PPPs on the market, which was for the products used for agricultural purposes, was published in the Official Journal (OJ) on 19 August 1991. The Directive 98/8/EC[2] concerning the placing of BPs on the market, which was for products used for non-agricultural purposes, was published in the OJ on 24 April 1998. An application for the approval of an AS under both the PPP Directive and the BP Directive required the submission of a dossier on at least one product containing the AS (Article 6 (2) of the Directive 91/414/EEC, Article 11 (1) (a) (ii) of the Directive 98/8/EC).

For authorisation of a product to be granted, an application for authorisation of a product submitted to a Member State, generally after the approval of the AS(s) included therein, is examined by the Member State, and any requirements laid down for authorisation are fulfilled, the Member State authorises the placing on the market and use of the product within the Member State (Article 4 (1) (a) of the Directive 91/414/EEC and Article 5 (1) (a) of the Directive 98/8/EC).

The PPP Directive 91/414/EEC was replaced by the PPP Regulation 1107/2009[3] published in the OJ on 24 November 2009, and the BP Directive 98/8/EC was replaced by the BP Regulation 528/2012[4] published in the OJ on 27 June 2012. Even under these new Regulations, a dossier on at least one product shall be included in an application for the approval or for purpose related to approval of an AS (Article 8 (1) (c) of the Regulation 1107/2009, Article 6 (1) (b) of the Regulation 528/2012).

Under the PPP Regulation 1107/2009, new provisions related to authorisation of products, according to which evaluation is conducted in each zone prior to evaluation by each Member State in the zone (Articles 35 and 36) were introduced. This zonal evaluation facilitates authorisation in other Member States through mutual recognition once a product is authorised in one Member State in a zone where agricultural, plant health and environmental conditions are comparable.

Under the PPP Regulation 1107/2009, a new provision on unacceptable co-formulants for inclusion in a product (Article 27) was also introduced. Pursuant to the provision, a list of co-formulants which are not accepted for inclusion in PPPs is included in Annex III (Article 27 (2)).

Under the BP Regulation 528/2012, a new provision of Union Authorisation (Article 41) was introduced for authorisation of products.

Applicants may apply for Union Authorisation for products which have similar conditions of use across the Union, with the exception of products that contain ASs meeting the exclusion criteria and those of product types (PTs) 14, 15, 17, 20 and 21, and the date from which Union Authorisation may be granted is specified (Article 42 (1)).

Products containing one or more new ASs are eligible for Union Authorisation from 1 September 2013 (date of application of the BP Regulation). For products containing only existing ASs, Union Authorisation will be available in three different stages, which are shown in **Table 1**.

The first Union Authorisation under the BP Regulation 528/2012 was published in the OJ in the form of the Regulation 2018/1258[5] on 21 September 2018. Although the Annex to the Regulation 2018/1258 did not contain information on non-active substances, the Union Authorisation Regulation 2018/1261[6], published in the OJ on the same 21 September 2018, contains information on non-active substances in the Annex, as shown in **Table 2**.

Under the BP Regulation, a new provision on eligibility

Table 1 Three different stages depending on the PT in which Union Authorisation will be available for BPs containing only existing ASs

When Union Authorisation will be available	PT number	PT
From 1 September 2013	1	Human hygiene
	3	Veterinary hygiene
	4	Food and feed area
	5	Drinking water
	18	Insecticides, acaricides and products to control other arthropods
	19	Repellents and attractants
From 1 January 2017	2	Disinfectants and algaecides not intended for direct application to humans or animals
	6	Preservatives for products during storage
	13	Working or cutting fluid preservatives
From 1 January 2020	7	Film preservatives
	8	Wood preservatives
	9	Fibre, leather, rubber and polymerised materials preservatives
	10	Construction material preservatives
	11	Preservatives for liquid-cooling and processing systems
	12	Slimicides
	16	Molluscicides, vermicides and products to control other invertebrates
	22	Embalming and taxidermist fluids

Table 2 Qualitative and quantitative information on the composition of the BP family Hypred's iodine based products indicated in Part I, Point 2.1 of the Annex to the Union Authorisation Regulation 2018/1261

Common name	IUPAC name	Function	CAS number	EC number	Content (%)	
					Min	Max
Iodine	(not indicated)	Active substance	7553-56-2	231-442-4	0.25	2.5
Alcohols, C12-14, ethoxylated (11 mol EO average molar ratio)	Poly(oxy-1,2-ethanediyl), -C12-14- (even numbered)-alkyl-hydroxy	Non-active substance	68439-50-9	(not indicated)	2.697	24.199

for the simplified authorisation procedure (Article 25) was also introduced.

To be eligible for the simplified authorisation procedure, a product must comply with all of the five conditions shown in **Table 3**. The first condition is that all the ASs contained in the product appear in Annex I of the BP Regulation 528/2012, *i.e.*, the substances do not give rise to concern. The second condition is that any substance of concern is not contained, *i.e.*, even non-active substances must not give rise to concern.

Although any specific provision indicating what conditions are considered to give rise to concern related to the substance of concern indicated in the second condition is not found, conditions which are considered to

Table 3 Conditions, if all of which are met, BP is eligible for the Simplified Authorisation procedure according to Article 25 of the BP Regulation 528/2012, and an application for authorisation may be made under a Simplified Authorisation procedure

Point	Condition
(a)	All the ASs contained in the BP appear in Annex I and satisfy any restriction specified in that Annex.
(b)	The BP does not contain any substance of concern.
(c)	The BP does not contain any nanomaterials.
(d)	The BP is sufficiently effective.
(e)	The handling of the BP and its intended use do not require personal protective equipment.

give rise to concern for the ASs listed in Annex I as indicated in the first condition are shown in **Table 4** (Article 28 (2)), so these conditions could also be considered to give rise to concern for non-active substances.

Under the BP Regulation 528/2012, such list as "List of co-formulants which are not accepted for inclusion in products" contained in Annex III to the PPP Regulation 1107/2009 is not provided, so whether non-active substances contained in a product is a substance that does not give rise to concern will be determined during the evaluation for authorisation.

2. Information required on co-formulants/non-active substances under the PPP/BP Directives and the PPP/BP Regulations

Information on co-formulants/non-active substances will be included in a dossier on product satisfying the data requirements for the authorisation of PPPs/BPs.

In order to reach the objective of the European Farm to Fork Strategy[7] of facilitating the placing on the market of biological ASs such as micro-organisms, Amendment Regulations were recently adopted which incorporate significant amendments to the PPP Regulation 1107/2009 and its related Regulations in which provisions relating to micro-organisms are included, and in the adopted Amendment Regulations an Amendment Regulation regarding data requirements for the authorisation of products based on which dossier is to be submitted, is included.

In this article, we omit information on the information requirements on co-formulants/non-active substances contained in products containing ASs that are micro-organisms, and focus on the information requirements for co-formulants/non-active substances contained in products containing chemical ASs.

Annex IIIA to the PPP Directive was to include data requirements for the dossier to be submitted for the authorisation of a PPP containing chemical AS(s), but when the PPP Directive 91/414/EEC was published in the OJ, only the titles of the points of the requirements were included. In the titles of the points of the requirements, indication related to co-formulants/non-active substances contained in products containing chemical ASs was found in the identity of the product and toxicological studies of the product. The contents of the requirements of the identity of the product were set

Table 4 Conditions according to which ASs are considered to give rise to concern and cannot be included in Annex I to the BP Regulation 528/2012

Point	Condition
(a)	ASs meet the criteria for classification according to the CLP Regulation 1272/2008 as: -explosive/highly flammable, -organic peroxide, -acutely toxic of category 1, 2 or 3, -corrosive of category 1A, 1B or 1C, -respiratory sensitiser, -skin sensitiser, -germ cell mutagen of category 1 or 2; -carcinogen of category 1 or 2, -human reproductive toxicant of category 1 or 2 or with effects on or via lactation, -specific target organ toxicant by single or repeated exposure, or -toxic to aquatic life of acute category 1.
(b)	ASs fulfil any of the substitution criteria set out in Article 10(1) 'An AS shall be considered a candidate for substitution if any of the following conditions are met: (a) it meets at least one of the exclusion criteria listed in Article 5(1) but may be approved in accordance with Article 5(2); (b) it meets the criteria to be classified, in accordance with the CLP Regulation, as a respiratory sensitiser; (c) its acceptable daily intake, acute reference dose or acceptable operator exposure level, as appropriate, is significantly lower than those of the majority of approved ASs for the same PT and use scenario; (d) it meets two of the criteria for being PBT in accordance with Annex XIII to REACH; (e) there are reasons for concern linked to the nature of the critical effects which, in combination with the use patterns, amount to use that could still cause concern, such as high potential of risk to groundwater, even with very restrictive risk management measures;or (f) it contains a significant proportion of non-active isomers or impurities.'
(c)	ASs have neurotoxic or immunotoxic properties.
	ASs also give rise to concern, even if none of the specific criteria in points (a) to (c) are met, where a level of concern equivalent to that arising from points (a) to (c) can be reasonably demonstrated based on reliable information.

out in Annex IIIA Point 1 to the PPP Directive by the Amendment Directive 94/37/EC[8] published in the OJ on 29 July 1994, and the contents of the requirements of toxicological studies of the product were set out in Annex IIIA Point 7 to the PPP Directive by the Amendment Directive 94/79/EC[9] published in the OJ on 31 December 1994.

With regard to analytical methods for products, there was no clear indication related to co-formulants/non-active substances contained in products containing chemical ASs in the titles of the points of the requirements, but the contents of the requirements for analytical methods for products were established in Annex IIIA Point 5 to the PPP Directive by the Amendment Directive 96/46/EC[10] published in the OJ on 23 August 1996. If requested, the methods for the determination of co-formulants or constituents of co-formulants in the product must be submitted.

Under the BP Directive 98/8/EC, Annex IIB contained the dossier requirements for the common core data set for the authorisation of BPs containing chemical ASs. The Annex to the BP Directive 98/8/EC contained only the titles of the points of the requirements, but the Guidance on data requirements for active substances and biocidal products dated October 2000[11] established specific details.

As shown in **Table 5**, there is not much difference between PPP and BP in terms of the information required

Table 5 Information on co-formulants/non-active substances required under the PPP Directive 91/414/EEC or the BP Directive 98/8/EC for the authorisation of products containing chemical ASs

Information	PPP Directive 91/414/EEC	BP Directive 98/8/EC
Content in the product	Annex IIIA 1.4.1*1	Annex IIB 2.2/GD*5 Annex IIB 2.2
Chemical name as given in Annex I to DSD	Annex IIIA 1.4.3 (if included in DSD)*1	(not indicated)
IUPAC/CA nomenclature	Annex IIIA 1.4.3 (if not included in DSD)*1	Annex IIB 2.2/GD*5 Annex IIB 2.2
Structure/Structural formula	Annex IIIA 1.4.3*1	Annex IIB 2.2/GD*5 Annex IIB 2.2
EC (EINECS/ELINCS) number	Annex IIIA 1.4.3*1	Annex IIB 2.2/GD*5 Annex IIB 2.2
CAS number	Annex IIIA 1.4.3*1	Annex IIB 2.2/GD*5 Annex IIB 2.2
Specification	Annex IIIA 1.4.3 (where the information provided does not fully identify a formulant)*1	Annex IIB 2.2/GD*5 Annex IIB 2.2 (if a non-active ingredient is a preparation)
Trade name	Annex IIIA 1.4.3 (where they exist)*1	Annex IIB 2.2/GD*5 Annex IIB 2.2
Function	Annex IIIA 1.4.4*1	Annex IIB 2.2/GD*5 Annex IIB 2.2
Classification (hazard classification)	(not required by Annex IIIA 1.4.3*1, but hazard classification is indicated in the SDS submitted as Document H)	Annex IIB 2.2/GD*5 Annex IIB 2.2 (according to DSD/according to DPD if a non-active ingredient is a preparation)
Methods for the determination of co-formulants or components of co-formulants/additives	Annex IIIA 5.1.2 (if required)*2	Annex IIB 4.2/GD*5 Annex IIB 4.2 (toxicologically and ecotoxicologically relevant components only)
Whether the substance is permitted in food, animal feeding stuffs, medicines or cosmetics	Document G*3	(no requirement)
Available toxicological data/information	Annex IIIA 7.4*4 Document I (where requested)*3	Annex IIB 6.5/GD*5 Annex IIB 6.5
Safety data sheet (SDS)	Annex IIIA 7.4*4 Document H*3	(not required by Annex IIB 6.5 or 7.3, but information from the SDS is to be submitted as available toxicological/ecotoxicological data/information)
Available ecotoxicological data/information	Document I (where requested)*3 (not required by Annex IIIA, but ecological information is indicated in the SDS submitted as Document H)	Annex IIB 7.3/GD*5 Annex IIB 7.3.1

DSD: Dangerous Substances Directive 67/548/EEC DPD: Dangerous Preparations Directive 88/379/EEC amended by 1999/45/EC
GD: Guidance Document
*1: Details of the required information introduced by the Amendment Directive 94/37/EC
*2: Details of the required information introduced by the Amendment Directive 94/46/EC
*3: Requirement introduced by the Amendment Directive 93/71/EEC, and complemented by European Commission Document 1663/VI/94
*4: Details of the required information introduced by the Amendment Directive 94/79/EC
*5: Details of the required information complemented by the Guidance Document

on co-formulants/non-active substances.

The IUPAC/CA nomenclature, content in the product, trade name, CAS/EC number, structure/structural formula, and function of the co-formulants/non-active substances are commonly required for co-formulants/non-active substances contained in PPPs/BPs.

For non-active substances contained in BPs, classification according to the Dangerous Substances Directive (DSD) 67/548/EEC[12] published in the OJ on 16 August 1967, is required.

The Introduction of Annex III to the PPP Directive 91/414/EEC was replaced by the Amendment Directive 93/71/EEC[13] published in the OJ on 31 August 1993. The newly introduced provisions introduce a provision that in individual cases it may be necessary to require certain information as provided for requirements for the approval of a chemical AS in Annex IIA to the PPP Directive, for co-formulants in the PPPs, and a provision that before such information will be required and before possible new studies have to be performed, all information on the co-formulant, made available to the competent authority of the Member State, will be considered, in particular when:

- The use of the co-formulant is permitted in food, animal feeding stuffs, medicines or cosmetics in accordance with Community Legislation.
- A safety data sheet (SDS) has been submitted for the co-formulant in accordance with the DS Directive 67/548/EEC.

Regarding analytical methods for the determination of co-formulants/non-active substances, they must be submitted for PPPs if required, and for BPs in so far as not covered by data set for the AS, analytical methods for toxicologically and ecotoxicologically relevant components of the BP and/or residues thereof is required, where relevant in or on PT-specific guidance.

Regarding toxicological data relating to co-formulants/non-active substances, there are requirements in the section of toxicological studies on PPP/BP, but their contents are slightly different.

Regarding ecotoxicological data relating to co-formulants/non-active substances, there are requirements in the section of ecotoxicological studies on BP, but there are no requirements in the section of ecotoxicological studies on PPP.

As shown in **Table 6**, toxicological and ecotoxicological data relating to co-formulants of PPP, along with other information, are to be submitted as Documents G to I, which are elements of the Individual Documents Required, as presented in "Guidelines and Criteria for the Preparation and Presentation of Complete Dossiers and of Summary Dossiers for the Inclusion of Active Substances in Annex I of Directive 91/414/EEC"[14].

A statement as to whether the co-formulant is permitted in food, animal feeding stuffs, medicines or cosmetics should be submitted as Document G, SDS as Document H, and, where requested, other available toxicological and environmental data should be submitted as Document I.

The classification of co-formulants according to the DS Directive 67/548/EEC is generally included in SDSs. Therefore, information on hazard classification is to be submitted through SDSs.

The PPP Directive 91/414/EEC was replaced by the PPP Regulation 1107/2009.

Certain provisions set out in the Annexes to the PPP

Table 6 Information on co-formulants required under the PPP Directive 91/414/EEC, as amended by the Amendment Directive 93/71/EEC, and complemented by European Commission Document 1663/VI/94 for the authorisation of products containing chemical ASs

Information	Directive 91/414/EEC as amended by Directive 93/71/EEC	Document 1663/VI/94*
Whether the substance is permitted in food, animal feeding stuffs, medicines or cosmetics	Annex III Introduction 4: The use of the formulant is permitted in food, animal feeding stuffs, medicines or cosmetics in accordance with Community legislation	Document G: A statement as to whether the substance is permitted in food, animal feeding stuffs, medicines or cosmetics in accordance with Community legislation
Safety data sheet (SDS)	Annex III Introduction 4: An SDS has been submitted for the co-formulant in accordance with the DSD 67/548/EEC	Document H: A copy of the SDS prepared in accordance with the DSD 67/548/EEC
Other available toxicological and environmental data	(not indicated)	Document I: Where requested, other available toxicological and environmental data

*: Document 1663/VI/94 'Guidelines and Criteria for the Preparation and Presentation of Complete Dossiers and of Summary Dossiers for the Inclusion of Active Substances in Annex I of Directive 91/414/EEC'

Directive 91/414/EEC were to be transferred into separate legal instruments to be adopted by the European Commission within 18 months after the entry into force of the PPP Regulation 1107/2009 on 14 December 2009 (twentieth day following its publication in the OJ), and a Regulation on data requirements for PPPs was to be adopted by 14 June 2011 (Article 84 (c) of the Regulation 1107/2009). The PPP Data Requirement Regulation 545/2011[15], published in the OJ on 11 June 2011, includes the content of the data requirements for the dossier to be submitted for the authorisation of a PPP in Annex III to the PPP Directive 91/414/EEC without any substantial modification.

Pursuant to the provision on amendments to the Regulation on data requirements for PPPs, taking into account current scientific and technical knowledge (Article 78 (1) (b) of the Regulation 1107/2009), the PPP Data Requirement Regulation 545/2011 was replaced by the PPP Data Requirement Regulation 284/2013[16] published in the OJ on 3 April 2013.

Even after the PPP Data Requirement Regulation 545/2011 was replaced by the PPP Data Requirement Regulation 284/2013, there were not significant changes regarding the information required for the co-formulants contained in PPPs, as shown in **Table 7**. However, the provision of SDSs pursuant to Article 31 of the

Table 7 Information on co-formulants required under the PPP Directive 91/414/EEC and under the PPP Regulation 1107/2009 (data requirements for PPP are set by the PPP Data Requirement Regulation 284/2013) for the authorisation of products containing chemical ASs

Information	PPP Directive 91/414/EEC	PPP Regulation 1107/2009
Content in the product	Annex IIIA 1.4.1*1	Annex Part A 1.4.1*5
Chemical name as given in Annex I to DSD/Part 3 of Annex VI to CLP Reg	Annex IIIA 1.4.3 (if included in DSD)*1	Annex Part A 1.4.3 (where possible)*5
IUPAC/CA nomenclature	Annex IIIA 1.4.3 (if not included in DSD)*1	Annex Part A 1.4.3 (if not included in CLP Reg)*5
Structure/Structural formula	Annex IIIA 1.4.3*1	Annex Part A 1.4.3*5
EC (EINECS/ELINCS) number	Annex IIIA 1.4.3*1	Annex Part A 1.4.3 (where exist)*5
CAS number	Annex IIIA 1.4.3*1	Annex Part A 1.4.3 (where exist)*5
Specification	Annex IIIA 1.4.3 (where the information provided does not fully identify a formulant)*1	Annex Part A 1.4.3 (where the information provided does not fully identify the co-formulant)*5
Trade name	Annex IIIA 1.4.3 (where they exist)*1	Annex Part A 1.4.3 (where available)*5
Function	Annex IIIA 1.4.4*1	Annex Part A 1.4.3*5
Classification (hazard classification)	(not required by Annex IIIA 1.4.3*1, but hazard classification is indicated in the SDS submitted as Document H)	(not required by Annex Part A 1.4.3*5, but hazard classification is indicated in the SDS submitted as Document H)
Methods for the determination of co-formulants or components of co-formulants	Annex IIIA 5.1.2 (if required)*2	Annex Part A 5.1.1 (where required by the national competent authorities)*5
Whether the substance is permitted in food, animal feeding stuffs, medicines or cosmetics	Document G*3	Document G*6
Available toxicological data/information	Annex IIIA 7.4*4 Document I (where requested)*3	Annex Part A 7.4*5 Document I (where requested)*6
Safety data sheet (SDS)	Annex IIIA 7.4*4 Document H*3	Annex Part A 1.4.3*5 Annex Part A 7.4*5 Document H*6
Available ecotoxicological data/information	Document I (where requested)*3 (not required by Annex IIIA, but ecological information is indicated in the SDS submitted as Document H)	Document I (where requested)*6 (not required by Annex Part A*5, but ecological information is indicated in the SDS submitted as Document H)

DSD: Dangerous Substances Directive 67/548/EEC CLP Reg: Classification, Labelling and Packaging Regulation 1272/2008
*1: Details of the required information introduced by the Amendment Directive 94/37/EC
*2: Details of the required information introduced by the Amendment Directive 94/46/EC
*3: Requirement introduced by the Amendment Directive 93/71/EEC, and complemented by European Commission Document 1663/VI/94
*4: Details of the required information introduced by the Amendment Directive 94/79/EC
*5: Requirement set out by the PPP Data Requirement Regulation 284/2013
*6: Documents to be included in a submission according to the Dossier Preparation Guidance Document SANCO/10181/2013

Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) Regulation 1907/2006[17], which was included in the introduction, is included not in the introduction but under the requirement point, namely Point 1.4.3 for products containing chemical ASs, together with a statement that SDSs shall be up to date and in accordance with other Union legislation.

However, Documents G to I remain as documents to be included in a submission according to the "Guidance Document for Applicants on preparing Dossiers for the Approval of a Chemical New Active Substance and for the Renewal of Approval of a Chemical Active Substance according to Regulation 283/2013 and Regulation 284/2013"[18] and the SDSs for co-formulants are submitted as Document H in the dossier.

The BP Directive 98/8/EC was replaced by the BP Regulation 528/2012.

The dossier requirements for the common core data set for authorisation of BPs containing chemical ASs set out in Annex IIB of the BP Directive 98/8/EC have been succeeded to Annex III Title 1 to the BP Regulation 528/2012. In Annex III Title 1 to the BP Regulation 528/2012, the Core Data Set of BPs containing chemical ASs set out in Annex IIB and the Additional Data Set for BPs containing chemical ASs set out in Annex IIIB to the BP Directive 98/8/EC are included in the same table. The details of each requirement are provided in the four guidance documents that deal with the information requirements, corresponding to Part A 'Information Requirements' of each of the four volumes, Vol. I to IV, by major areas as shown in **Table 8**.

Significant changes were not introduced with respect to the information required for non-active substances contained in BP. The DS Directive 67/548/EEC, which was the legislation for classification and labelling of chemical substances, has been replaced by the Classification, Labelling and Packaging (CLP) Regulation 1272/2008[19] published in the OJ on 31 December 2008, which changed the evaluation procedure for establishing/revising classification and labelling.

Under the CLP Regulation, substances that fulfil the criteria for hazard classes referred to in Article 36 (1) and ASs of PPPs or BPs [Article 36 (2) of the Regulation 1272/2008] are normally subject to EU harmonised classifications and labelling (CLH). If a substance that is not an AS of PPP or BP fulfills the criteria for other hazard classes than those referred to in Article 36 (1), CLH may be set on a case-by-case basis, if justification is provided demonstrating the need for CLH setting at Community level (Article 36 (3) of the Regulation 1272/2008).

Impact of concerns related to co-formulants/non-active substances contained in PPPs/BPs on authorisation/renewal of authorisation of PPPs/BPs

1. Impact of concerns related to co-formulants contained in PPPs on authorisation/renewal of authorisation of PPPs

As mentioned above, the PPP Regulation 1107/2009 introduced new provisions regarding unacceptable co-formulants in products, and unacceptable co-formulants were to be listed in Annex III, list of co-formulants which are not accepted for inclusion in PPPs. This list was established by the Amendment Regulation 2021/383[20] published in the OJ on 4 March 2021.

Co-formulants are used together with ASs in products and are thus equally spread in the environment. Therefore, the criteria for the approval of ASs provided for in points 3.6.2, 3.6.3, 3.6.4, 3.6.5, 3.7, 3.8.2 and 3.10 of Annex II to the PPP Regulation 1107/2009, should also be relevant to identify unacceptable co-formulants.

Table 9 shows the criteria for the approval of ASs that are also relevant to identify unacceptable co-formulants.

Other than the substances of concern related to the criteria for the approval of ASs mentioned above, the substances listed in Annex III to the PPP Regulation by the Amendment Regulation 2021/383 include substances identified as substances of concern in accordance

Table 8 ECHA Guidances that describe how to fulfil the information requirements set by the BP Regulation 528/2012

Vol. number	Part(s) covered	Title of Guidance
Volume I	Parts A + B + C	Identity of the active substance/physico-chemical properties/analytical methodology – Information Requirements, Evaluation and Assessment
Volume II	Part A	Efficacy - Information Requirements
Volume III	Part A	Human health - Information Requirements
Volume IV	Part A	Environment - Information Requirements

Table 9 Criteria provided for in points of Annex II to the PPP Regulation 1107/2009 that are relevant to identify unacceptable co-formulants

Point	Concern	Criteria for the approval of ASs
3.6.2	Mutagenicity	Not to be classified as mutagen category 1A or 1B[#]
3.6.3[+]	Carcinogenicity	Not to be classified as carcinogen category 1A or 1B[#*1]
3.6.4[+]	Reproductive toxicity	Not to be classified as toxic for reproduction category 1A or 1B[#*1]
3.6.5[+]	Endocrine disrupting properties for humans	Not considered to have endocrine disrupting properties that may cause adverse effects in humans[#*1]
3.7	Fate and behaviour in the environment - POP, PBT, vPvB	Not considered to be a persistent organic pollutant (POP)[#] Not considered to be a persistent, bioaccumulative and toxic (PBT) substance[#] Not considered to be a very persistent and very bioaccumulative substance (vPvB)[#]
3.8.2[+]	Endocrine disrupting properties for non-target organisms	Not considered to have endocrine disrupting properties that may cause adverse effects on non-target organisms[#*2]
3.10	Fate and behaviour concerning groundwater	Predicted concentration of the AS or of metabolites, degradation or reaction products in groundwater complies with the respective criteria of the uniform principles

+: According to Article 4(7), an AS may be approved for a limited period necessary to control a serious danger to plant health which cannot be contained by other available means but not exceeding five years even if it does not satisfy the criteria set out in points 3.6.3, 3.6.4, 3.6.5 or 3.8.2 of Annex II, provided that the use of the AS is subject to risk mitigation measures to ensure that exposure of humans and the environment is minimised.

#: So-called 'Cut-off' criteria. According to Article 4(1), the assessment of the AS shall first establish whether the approval criteria set out in points 3.6.2 to 3.6.4 and 3.7 of Annex II are satisfied. If these criteria are satisfied, the assessment shall continue to establish whether the other approval criteria set out in points 2 and 3 of Annex II are satisfied.

*1: Unless the exposure of humans to that AS in a PPP, under realistic proposed conditions of use, is negligible, that is, the PPP is used in closed systems or in other conditions excluding contact with humans and where residues of the AS concerned on food and feed do not exceed the default value set in accordance with Article 18(1)(b) of the MRL Regulation 396/2005

*2: Unless the exposure of non-target organisms to that AS in a PPP under realistic proposed conditions of use is negligible

with the CLP Regulation 1272/2008, the REACH Regulation 1907/2006, and other Regulations. **Table 10** lists the concerns related to the substances listed in Annex III to the PPP Regulation and the Regulations in accordance with which those concerns were identified.

Co-formulants listed in Annex III to the PPP Regulation may be present as unintentional impurities in other co-formulants, which as such are acceptable for use in PPPs. Therefore, the individual concentration of the unacceptable co-formulants in the finished PPP should be less than 0.1% w/w in order to be considered as an acceptable unintentional impurity, unless a different limit is provided due to technical limitations of relevant analysis methods. Where a specific concentration limit related to carcinogenic/mutagenic/reprotoxic properties established in Annex VI to the CLP Regulation 1272/2008 for the unacceptable co-formulant is at a level lower than 0.1% w/w, the individual concentration should be less than the specific concentration limit.

The Amendment Regulation 2021/383 entered into force on 24 March 2021, twentieth day following its publication in the OJ, 4 March 2021 (Article 5).

The Amendment Regulation 2021/383 provides that Member States which have granted authorisations for PPPs containing co-formulants listed in Annex III to the PPP Regulation shall amend or withdraw those authorisations as soon as possible but no later than 24 March 2023, two years from the entry into force of the Amendment Regulation (Article 2). If a substance contained in a product is listed in Annex III to the PPP Regulation as an unacceptable co-formulant, authorisation for the product granted by Member States will be withdrawn unless the authorisation is amended by an application for amendment of the authorisation.

The European Commission may review co-formulants at any time. It may take into account relevant information provided by Member States (Article 27 (3) of the Regulation 1107/2009).

2. Impact of concerns related to non-active substances contained in BPs on authorisation/renewal of authorisation of BPs

As mentioned above, under the BP Regulation 528/2012, there is no such list as "List of co-formulants which are not accepted for inclusion in PPPs" provided in Annex III to the PPP Regulation 1107/2009, so it will be determined during the evaluation for authorisation whether the non-active substances have been evaluated

Table 10 Concerns of the substances, other than those related to the criteria provided for in Points of Annex II to the PPP Regulation 1107/2009, which also are relevant to identify unacceptable co-formulants to be included in Annex III to the PPP Regulation 1107/2009 amended by the Amendment Regulation 2021/383

Concern	Substances to be included in the list of unacceptable co-formulants
Classification (hazard classification and hazard category)	Substances with a harmonised classification as carcinogens, category 1A or 1B, as mutagens, category 1A or 1B, or as toxic to reproduction, category 1A or 1B, in accordance with Annex VI to the CLP Regulation 1272/2008
PBT/vPvB	Substances identified as PBT (persistent, bioaccumulative and toxic) or vPvB (very persistent and very bioaccumulative) in accordance with points (d) and (e) of Article 57 of REACH
Endocrine disrupting properties	Substances of very high concern due to endocrine disrupting properties in accordance with point (f) of Article 57 of REACH or substances identified as endocrine disruptors under the BP Regulation 528/2012
POP	Substances identified as POP (persistent organic pollutants) under the POP Regulation 2019/1021
Restrictions on use (Annex XVII to REACH)	The use of substances is subject to restrictions under REACH as co-formulants in PPPs
Prohibition of use (Conditions of approval of an AS)	The use of polyethoxylated tallowamines (CAS number 61791-26-2) in PPPs containing glyphosate was prohibited by the Amendment of conditions of approval Regulation 2016/1313*1, as concerns were identified in relation to the toxicity of polyethoxylated tallowamines and their potential to negatively affect human health (given that those concerns are due to the intrinsic properties of the substances concerned and are thus not limited to formulated products containing glyphosate but are equally valid for formulated products containing other ASs)
Not approved ASs for use in BP	PHMB (1600; 1.8), CAS number 27083-27-8 and 32289-58-0, which were not approved for PTs1 (Human hygiene), 6 (Preservatives for products during storage) and 9 (Fibre, leather, rubber and polymerised materials preservatives) by non-approval Decision 2016/109*2, and PHMB (1415; 4.7), CAS number 32289-58-0 and 1802181-67-4, which were not approved for PTs1, 5 (Drinking water) and 6 by non-approval Decision 2018/619*3, due to unacceptable risks for human health and the environment (their use as preservatives in PPPs would, therefore, lead to unacceptable effects on human health and the environment)

*1: Commission Implementing Regulation (EU) 2016/1313 of 1 August 2016 amending Implementation Regulation (EU) No 540/2011 as regards the conditions of approval of the active substance glyphosate

*2: Commission Implementing Decision (EU) 2016/109 of 27 January 2016 not to approve PHMB (1600; 1.8) as an existing active substance for use in biocidal products for product-types 1, 6 and 9

*3: Commission Implementing Decision (EU) 2018/619 of 20 April 2018 not approving PHMB (1415; 4.7) as an existing active substance for use in biocidal products of product-types 1, 5 and 6

under REACH or other Regulations and whether the non-active substances do not give rise to concern taking into consideration the outcome of evaluation or status of evaluation.

The Union Authorisation Regulation 2020/704[21], published in the OJ on 27 May 2020, includes a recital in which a non-active substance identified as potentially having concerns is disclosed and stated that the Union Authorisation has to be cancelled or amended if it is eventually concluded that the non-active substance is considered as having such concerns.

As shown in **Table 11**, when compared the information on the non-active substances listed in Annex to the Regulation 2020/704 with the information on the non-active substance identified as having concerns, even the presence of very low level of the non-active substance is considered to have an impact on the authorisation of products.

The Biocidal Products Committee (BPC) Opinion dated 26 June 2019[22] on the Union Authorisation of BP mentioned above did not disclose the name of the non-active substance identified as having concerns, but it did state that a process under the REACH Regulation will be triggered for the substance.

Impact of "One substance-one assessment" planned in the Chemicals Strategy on authorisation/renewal of authorisation of PPPs/BPs related to co-formulants/non-active substances contained in PPPs/BPs

"Chemicals Strategy for Sustainability-Towards a Toxic-Free Environment" published on 14 October 2020[23] presents an action plan in which there are proposals, such as establishment of a "One substance-one assessment" process to coordinate the hazard/risk assessment on chemicals across chemical legislation, through the use of an expert group and a Commission coordination mechanism, amendment of CLP Regulation, and horizontal proposal to remove legislative

Table 11 Qualitative and quantitative information on the composition of the BP family 'INSECTICIDES FOR HOME USE' indicated in Annex II to the Union Authorisation Regulation 2020/704

Common name	IUPAC name	Function	CAS number	EC number	Content (%)	
					Min	Max
Permethrin	(not indicated)	Active Substance	52645-53-1	258-067-9	0.177	0.177
S-Methoprene	(not indicated)	Active Substance	65733-16-6	(not indicated)	0.00225	0.00225
Propan-2-ol	Propan-2-ol	Non-active substance	67-63-0	200-661-7	3.33475	3.33475
n-butane	n-butane	Non-active substance	106-97-8	203-448-7	63.458	63.458
propane	propane	Non-active substance	74-98-6	200-827-9	16.271	16.271
isobutane	isobutane	Non-active substance	75-28-5	200-857-2	4.068	4.068
Nitromethane*	Nitromethane**	Non-active substance**	75-52-5**	200-876-6**	***	***

*: As regards the non-active substance nitromethane contained in the BP family 'INSECTICIDES FOR HOME USE', it was not possible to conclude whether it meets the scientific criteria for the determination of endocrine-disrupting properties set out in the BP ED Criteria Regulation 2017/2100 within the period for the evaluation of the application.

**: This information is not indicated in Annex II to the Union Authorisation Regulation 2020/704.

***: No information

obstacles for re-use of data, to streamline the data flow across legislation and to extend the open data and transparency principles from the EU food safety sector to other pieces of chemical legislation. Proposal to amend the CLP Regulation includes the introduction of new hazard classes on Endocrine Disrupting properties (ED), Persistent, Bioaccumulative and Toxic (PBT), Very Persistent and Very Bioaccumulative (vPvB), *etc*.

As mentioned above co-formulants/non-active substances that are registered/authorised under the REACH Regulation or are ASs of PPPs/BPs which are regarded as registered under REACH, are normally subject to CLH and CLH of the substances have been established if they fulfill the criteria for hazard classes specified in the CLP Regulation. If CLH of the substances has not yet been established because a proposal for CLH is to be submitted/being evaluated, there is self-classification of the substances until CLH of the substances is established.

If new hazard classes on ED, PBT and vPvB are introduced, a proposal for CLH setting/revising of a substance that could fulfill the criteria of any of these hazard classes would be submitted.

Even if a substance has been registered/authorised under the REACH Regulation in the past, it may be considered to have ED properties if the assessment was carried out in line with the ED criteria that were not set out at that time. As a result, if the substance is included in the list of co-formulants which are not accepted for inclusion in PPPs in Annex III to the PPP Regulation 1107/2009, authorisation granted for a product containing the substance as co-formulant may be withdrawn unless an application for amendment of authorisation to replace the unacceptable co-formulant with another equivalent co-formulant is assessed and the authorisation is amended.

In the case of Union Authorisation under the BP Regulation 528/2012, if a non-active substance is identified as meeting ED criteria, the non-active substance becomes a substance of concern, and because of the concern a Union Authorisation may not be granted or conditions may be imposed on the authorisation. In the case of a product authorised according to the simplified authorisation procedure or applied for authorisation under the simplified authorisation procedure, if a non-active substance is identified as meeting ED criteria, it will no longer be eligible for the simplified authorisation procedure and cancellation of the authorisation or withdrawal of the application for authorisation may be decided.

Conclusion

Under the initial EU legislation for PPP/BP, application for authorisation of product after approval/renewal of approval of ASs was evaluated by each Member State, and the assessment of concerns present in co-formulants/non-active substances contained in the products assessed for authorisation/renewal of authorisation might differ among Member States, thus the assessment was not always harmonised within the Union. Recently, the list of co-formulants which are not accepted for inclusion in PPPs in Annex III introduced by the PPP Regulation 1107/2009, was established. Furthermore, it has only recently been found that non-active substance concerns are assessed during the evaluation

for Union Authorisation introduced by the BP Regulation 528/2012, and the concerns identified may have an impact on the authorisation of products.

In order to ensure that authorisation/renewal of authorisation of PPPs/BPs are granted, it is necessary to investigate concerns that co-formulants/non-active substances contained in the product may give rise to. It is necessary to foresee concerns that may arise as an outcome of assessment not only through information included in SDSs provided by suppliers of co-formulants/non-active substances and the outcome of previous assessment under the REACH Regulation and other Regulations, but also through information published in the course of ongoing evaluation of co-formulants/non-active substances.

In cases where it is foreseeable that because of the concerns about co-formulants/non-active substances contained in PPPs/BPs authorisation/renewal of authorisation of the product becomes difficult to be granted, or conditions may be imposed, alternative co-formulants/non-active substances should be sought if necessary and provide products equivalent to the ones for which authorisations were granted or applications for authorisation have been submitted. Information must be gathered as soon as possible in order to support the authorisation of products and avoid the imposition of conditions by replacing them with equivalent products. We would be pleased if this article is of assistance in dealing with such work. In the section 'Reference', the links to the referenced documents are also provided, as far as they are currently available, so that the details can be confirmed with the contents of the document.

Reference

1) EC, "Directive 91/414/EEC (OJ 1991.08.19)", https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:31991L0414&from=EN (Ref. 2022/3/29).
2) EC, "Directive 98/8/EC (OJ 1998.04.24)", https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:31998L0008&from=EN (Ref. 2022/3/29).
3) EC, "Regulation 1107/2009 (OJ 2009.11.24)", https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32009R1107&from=EN (Ref. 2022/3/29).
4) EU, "Regulation 528/2012 (OJ 2012.06.27)", https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32012R0528&from=EN (Ref. 2022/3/29).
5) EU, "Regulation 2018/1258 (OJ 2018.09.21)", https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32018R1258&from=EN (Ref. 2022/3/29).
6) EU, "Regulation 2018/1261 (OJ 2018.09.21)", https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32018R1261&from=EN (Ref. 2022/3/29).
7) European Commission, "A Farm to Fork Strategy for a fair, healthy and environmentally-friendly food system, COM(2020) 381 final, 2020.05.20", https://eur-lex.europa.eu/resource.html?uri=cellar:ea0f9f73-9ab2-11ea-9d2d-01aa75ed71a1.0001.02/DOC_1&format=PDF Text (Ref. 2022/3/29). https://eur-lex.europa.eu/resource.html?uri= cellar:ea0f9f73-9ab2-11ea-9d2d-01aa75ed71a1.0001.02/DOC_2&format=PDF, Annex (Ref. 2022/3/29).
8) EC, "Directive 94/37/EC (OJ 1994.07.29)", https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:31994L0037&from=EN (Ref. 2022/3/29).
9) EC, "Directive 94/79/EC (OJ 1994.12.31)", https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:31994L0079&from=EN (Ref. 2022/3/29).
10) EC, "Directive 96/46/EC (OJ 1996.08.23)", https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:31996L0046&from=EN (Ref. 2022/3/29).
11) European Commission, "Guidance on data requirements for active substances and biocidal products, 2000.10, formatted and edited in one single document 2008.02", https://echa.europa.eu/documents/10162/983772/bpd_guid_tnsg-data-requirements_en.pdf/48dcca8e-54b4-46e2-9b66-b6bab8e6a26e (Ref. 2022/3/29).
12) EC, "Directive 67/548/EEC (OJ 1967.08.16)", https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:31967L0548&from=EN (Ref. 2022/3/29).
13) EC, "Directive 93/71/EEC (OJ 1993.08.31)", https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:31993L0071&from=EN (Ref. 2022/3/29).
14) European Commission, "Guidelines and Criteria for the Preparation and Presentation of Complete Dossiers and of Summary Dossiers for the Inclusion of Active Substances in Annex I of Directive 91/414/EEC (Article 5.3 and 8.2), Document 1663/VI/94", which has been replaced several times by updated versions, the latest updated version is Rev. 8 dated 22 April 1998.
15) EU, "Regulation 545/2011 (OJ 2011.06.11)", https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32011R0545&from=EN (Ref. 2022/3/29).
16) EU, "Regulation 284/2013 (OJ 2013.04.03)", https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32013R0284&from=EN (Ref. 2022/3/29).

17) EC, "Regulation 1907/2006, (OJ 2006.12.30)", https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32006R1907&from=EN (Ref. 2022/3/29). "Corrigendum to Regulation 1907/2006 (OJ 2007.05.29)", https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32006R1907R(01)&from=EN (Ref. 2022/3/29).
18) European Commission, "Guidance Document for Applicants on preparing Dossiers for the Approval of a Chemical New Active Substance and for the Renewal of Approval of a Chemical Active Substance according to Regulation (EU) No 283/2013 and Regulation (EU) No 284/2013, SANCO/10181/2013", which has been replaced several times by updated versions, the first one probably being Rev. 1 dated 15 March 2013, and the latest updated version is Rev. 6 dated 24 March 2021, https://ec.europa.eu/food/system/files/2021-03/pesticides_ppp_app-proc_guide_doss_10181.pdf (Ref. 2022/3/29).
19) EC, "Regulation 1272/2008 (OJ 2008.12.31)", https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32008R1272&from=EN (Ref. 2022/3/29).
20) EU, "Regulation 2021/383 (OJ 2021.03.04)", https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32021R0383&from=EN (Ref. 2022/3/29).
21) EU, "Regulat ion 2020/704 (OJ 2020.05.27)", https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32020R0704&from=EN (Ref. 2022/3/29).
22) European Chemicals Agency, "Biocidal Products Committee (BPC) Opinion on the Union authorisation of the biocidal product family: INSECTICIDES FOR HOME USE, ECHA/BPC/228/2019, 2019.06.26", https://echa.europa.eu/documents/10162/2166576/Insecticides+for+home+use_Final+BPC+opinion.pdf (Ref. 2022/3/29).
23) European Commission, "Chemicals Strategy for Sustainability-Towards a Toxic-Free Environment, COM(2020) 667 final, 2020.10.14", https://eur-lex.europa.eu/resource.html?uri=cellar:f815479a-0f01-11eb-bc07-01aa75ed71a1.0003.02/DOC_1& format=PDF Text (Ref. 2022/3/29).
https://eur-lex.europa.eu/resource.html?uri=cellar:f815479a-0f01-11eb-bc07-01aa75ed71a1.0003.02/DOC_2&format=PDF, Annex (Ref. 2022/3/29).

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